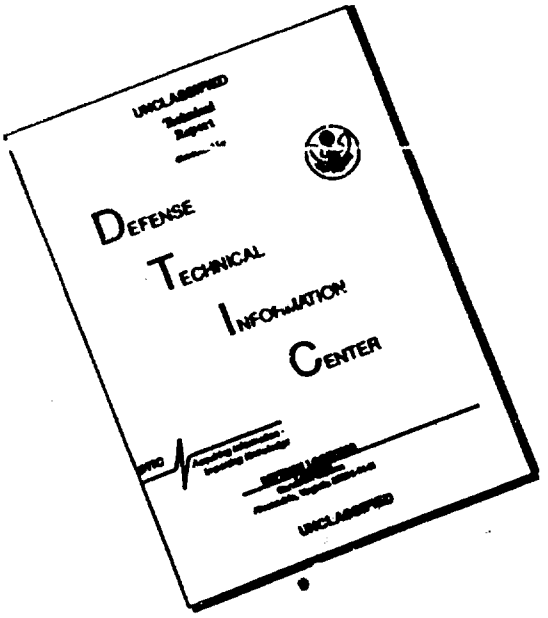
EVALUATION OF GROUP C MENINGOCOCCAL POLYSACCHARIDE VACCINE IN MARINE RECRUITS, SAN DIEGO, CALIFORNIA

Leonard F. Devine, et al

Naval Medical Research Unit No. 4
Great Lakes, Illinois

29 December 1969

DISCLAIMER NOTICE



THIS DOCUMENT IS BEST QUALITY AVAILABLE. THE COPY FURNISHED TO DTIC CONTAINED A SIGNIFICANT NUMBER OF PAGES WHICH DO NOT REPRODUCE LEGIBLY.

UNCLASSIFIED
Security Classification

AD-769364

DOCUMENT CONTROL DATA - R&D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1. ORIGINATING ACTIVITY (Corporate author)
Naval Medical Research Unit No. 4
Great Lakes, Illinois 60088

2a. REPORT SECURITY CLASSIFICATION
Unclassified

2b. GROUP

3. REPORT TITLE
Evaluation of Group C Meningococcal Polysaccharide Vaccine in Marine Recruits, San Diego, California

4. DESCRIPTIVE NOTES (Type of report and inclusive dates)
Final

5. AUTHOR(S) (Last name, first name, initial)
Devine, L. F., Pierce, W. E., Floyd, T. M., Rhode, S. L., Edwards, E. A. Siess, E. E., and Peckinpaugh, R. O.

6. REPORT DATE	7a. TOTAL NO. OF PAGES	7b. NO. OF REFS
July 1970	~~8~~ 11	10

8a. CONTRACT OR GRANT NO.	9a. ORIGINATOR'S REPORT NUMBER(S)
b. PROJECT NO. M4305.01-1016B	RU 69.23
c.	9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)
d.	

10. AVAILABILITY/LIMITATION NOTICES
Distribution of this document in unlimited.

11. SUPPLEMENTARY NOTES	12. SPONSORING MILITARY ACTIVITY
	Bureau of Medicine and Surgery Navy Department Washington, D. C.

13. ABSTRACT

Group C meningococcal polysaccharide vaccine was well tolerated by 3,018 vaccinated Marine recruits. The vaccine appeared to be group-specific since it prevented the acquisition of only group C meningococci. The vaccine stimulated a good hemagglutinating antibody response, but did not stimulate a complement fixing antibody response. One systemic illness of uncertain etiology, possibly vaccine related, was observed among the vaccinees. That the vaccine affords protection against clinical disease was suggested when three cases of meningococcal disease of group C etiology developed in the nonvaccinated controls while none occurred among the vaccinated men of the study population.

DD FORM 1 JAN 64 1473

UNCLASSIFIED
Security Classification

UNCLASSIFIED

Security Classification

14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Neisseria meningitidis group C meningococcal polysaccharide vaccine epidemiology meningococcal carriers hemagglutinating and complement-fixing meningococcal antibodies						

INSTRUCTIONS

1. ORIGINATING ACTIVITY: Enter the name and address of the contractor, subcontractor, grantee, Department of Defense activity or other organization *(corporate author)* issuing the report.

2a. REPORT SECURITY CLASSIFICATION: Enter the overall security classification of the report. Indicate whether "Restricted Data" is included. Marking is to be in accordance with appropriate security regulations.

2b. GROUP: Automatic downgrading is specified in DoD Directive 5200.10 and Armed Forces Industrial Manual. Enter the group number. Also, when applicable, show that optional markings have been used for Group 3 and Group 4 as authorized.

3. REPORT TITLE: Enter the complete report title in all capital letters. Titles in all cases should be unclassified. If a meaningful title cannot be selected without classification, show title classification in all capitals in parenthesis immediately following the title.

4. DESCRIPTIVE NOTES: If appropriate, enter the type of report, e.g., interim, progress, summary, annual, or final. Give the inclusive dates when a specific reporting period is covered.

5. AUTHOR(S): Enter the name(s) of author(s) as shown on or in the report. Enter last name, first name, middle initial. If military, show rank and branch of service. The name of the principal author is an absolute minimum requirement.

6. REPORT DATE: Enter the date of the report as day, month, year; or month, year. If more than one date appears on the report, use date of publication.

7a. TOTAL NUMBER OF PAGES: The total page count should follow normal pagination procedures, i.e., enter the number of pages containing information.

7b. NUMBER OF REFERENCES: Enter the total number of references cited in the report.

8a. CONTRACT OR GRANT NUMBER: If appropriate, enter the applicable number of the contract or grant under which the report was written.

8b, 8c, & 8d. PROJECT NUMBER: Enter the appropriate military department identification, such as project number, subproject number, system numbers, task number, etc.

9a. ORIGINATOR'S REPORT NUMBER(S): Enter the official report number by which the document will be identified and controlled by the originating activity. This number must be unique to this report.

9b. OTHER REPORT NUMBER(S): If the report has been assigned any other report numbers *(either by the originator or by the sponsor)*, also enter this number(s).

10. AVAILABILITY/LIMITATION NOTICES: Enter any limitations on further dissemination of the report, other than those imposed by security classification, using standard statements such as:

(1) "Qualified requesters may obtain copies of this report from DDC."

(2) "Foreign announcement and dissemination of this report by DDC is not authorized."

(3) "U. S. Government agencies may obtain copies of this report directly from DDC. Other qualified DDC users shall request through _____."

(4) "U. S. military agencies may obtain copies of this report directly from DDC. Other qualified users shall request through _____."

(5) "All distribution of this report is controlled. Qualified DDC users shall request through _____."

If the report has been furnished to the Office of Technical Services, Department of Commerce, for sale to the public, indicate this fact and enter the price, if known.

11. SUPPLEMENTARY NOTES: Use for additional explanatory notes.

12. SPONSORING MILITARY ACTIVITY: Enter the name of the departmental project office or laboratory sponsoring *(paying for)* the research and development. Include address.

13. ABSTRACT: Enter an abstract giving a brief and factual summary of the document indicative of the report, even though it may also appear elsewhere in the body of the technical report. If additional space is required, a continuation sheet shall be attached.

It is highly desirable that the abstract of classified reports be unclassified. Each paragraph of the abstract shall end with an indication of the military security classification of the information in the paragraph, represented as (TS), (S), (C), or (U).

There is no limitation on the length of the abstract. However, the suggested length is from 150 to 225 words.

14. KEY WORDS: Key words are technically meaningful terms or short phrases that characterize a report and may be used as index entries for cataloging the report. Key words must be selected so that no security classification is required. Identifiers, such as equipment model designation, trade name, military project code name, geographic location, may be used as key words but will be followed by an indication of technical context. The assignment of links, roles, and weights is optional.

DD FORM 1 JAN 64 1473 (BACK)

UNCLASSIFIED

AMERICAN JOURNAL OF EPIDEMIOLOGY Vol. 92, No. 1

EVALUATION OF GROUP C MENINGOCOCCAL POLYSACCHARIDE VACCINE IN MARINE RECRUITS, SAN DIEGO, CALIFORNIA[1]

LEONARD F. DEVINE[2], WILLARD E. PIERCE[3], THOMAS M. FLOYD[4] SOLON L. RHODE[5], EARL A. EDWARDS[6], EUGENE E. SIESS[7] AND ROBERT O. PECKINPAUGH[8]

(Received for publication December 29, 1969)

Devine, L. F., W. E. Pierce, T. M. Floyd, S. L. Rhode, E. A. Edwards, E. E. Siess and R. O. Peckinpaugh (Naval Medical Research Unit No. 4, Great Lakes, Illinois 60088). Evaluation of group C meningococcal polysaccharide vaccine in Marine recruits, San Diego, California. *Amer. J. Epid.*, 1970, 92: 25–32.— Group C meningococcal polysaccharide vaccine was administered to 3,018 Marine recruits. The vaccine appeared to be group-specific since it prevented the acquisition of only group C meningococci. The vaccine stimulated a good hemagglutinating antibody response, but did not stimulate a complement fixing antibody response. One systemic illness of uncertain etiology, possibly vaccine related, was observed among the vaccinees. That the vaccine affords protection against clinical disease was suggested when three cases of meningococcal disease of group C etiology developed in the nonvaccinated controls while none occurred among the vaccinated men of the study population.

antibodies; carrier state; complement fixation tests; hemagglutination inhibition tests; meningococcal infections; *Neisseria meningitidis*; recruits; vaccine, group C meningococcal polysaccharide

Until recently, attempts to develop an effective meningococcal vaccine for use in epidemic emergencies have met with limited success. Lepeysonnie, in 1963 (1), has reviewed the generally disappointing experience with immunization against meningococcal disease in Africa between 1915 and 1950. However, improvements in our understanding of natural immunity to meningococcus (2, 3) and the recent development of immunogenic group-specific meningococcal polysaccharide vaccines have

[1] From Naval Medical Research Unit No. 4 (NAMRU-4), Great Lakes, Illinois and Preventive Medicine Unit No. 5 (PMU-5), San Diego, Calif. This study was done in connection with Research Project No. M4305.01-1016B, Bureau of Medicine and Surgery, Navy Department, Wash., D. C. The opinions and assertions contained herein are those of the authors and are not to be construed as official or as reflecting the views of the Navy Department or the Naval Service at large. The use of commercially available products does not imply endorsement of, nor preference for the products.

Reprint request to: Commanding Officer, Naval Medical Research Unit No. 4, Great Lakes, Illinois 60088.

[2] Chief, Bacteriology Division, NAMRU-4.
[3] Chief, Biometrics Division, NAMRU-4.
[4] Bacteriologist, PMU-5, San Diego, Calif.
[5] Epidemiology Division, NAMRU-4.
[6] Chief, Immunology Division, NAMRU-4.
[7] Officer in Charge, PMU-5, San Diego, Calif.
[8] Commanding Officer, NAMRU-4.

The authors are indebted to the personnel of Preventive Medicine Unit #5, San Diego, Calif.: LCDR Richard L. Nail, MC USN, HMC M. J. Amos, HM1 L. F. Parsons, HM3 D. Rullcoski, HM3 M. Thompson, HM3 D. McLeod and HM3 G. P. Bond for technical assistance; to the personnel of Naval Medical Research Unit No. 4, Great Lakes, Illinois: Mr. G. L. Larson, HMC D. J. Seibert, HM1 J. Hannah, HM2 D. Mueller and Miss P. Muehl for technical and field assistance; to HM2 D. C. Herman and Mrs. B. Kubik for biometric assistance; and to Mr. C. E. Knight, Mrs. L. M. Duggan and Mrs. P. C. Warren for assistance in preparation of the manuscript.

improved the prospects for interrupting the spread of meningococci in populations at risk (4–6). An opportunity to further evaluate the group C polysaccharide vaccine of Gotschlich et al. (4) occurred at the Marine Corps Recruit Depot (MCRD), San Diego, California in April, 1969. Clinical cases of meningococcal disease caused by group C meningococci began to occur frequently in Marine recruits at MCRD during 1968. There were 16 bacteriologically confirmed cases caused by group C meningococci in that year. Twenty more cases caused by the same serogroup occurred in the first four months of 1969. Extensive meningococcal surveys conducted in March and April, 1969, showed that the group C carrier rate among recruits regularly increased from 5 per cent at the beginning of training to more than 40 per cent four weeks later. Accordingly, the decision was made to administer meningococcal polysaccharide vaccine to a portion of volunteers commencing Marine recruit training to determine the effect of vaccine on the spread of nasopharyngeal meningococci.

Materials and methods

The study population consisted of all Marine recruits entering training at the MCRD from April 28 to June 4, 1969. Approximately 1,000 men arrived weekly for eight weeks of basic training. Each day, arrivals were divided into platoons consisting of 75 to 80 men. Four consecutive platoons constituted a training series. Each series of platoons was assigned to one of the three battalions. Each battalion received at least one or more series of platoons per week. The first four weeks of training were accomplished at the MCRD. The integrity of each platoon was maintained during these four weeks and the opportunity for contact with other platoons was minimal. The men were relocated in another camp at the end of the fourth week for two weeks of training on the rifle range. The berthing facilities at this camp did not permit separation of platoons or series. Hence, the men from various platoons and series commingled freely in the fifth and sixth week of training. During the study, routine immunization and prophylactic procedures were continued without interruption. Included were sulfisoxazole 1 gm twice daily by mouth for two days upon arrival (to eliminate sulfadiazine-sensitive meningococcal strains) and benzathine penicillin G 1,200,000 units intramuscularly in the second week of training (to eliminate and prevent subsequent acquisition of group A streptococci).

Platoons were randomly preselected to be vaccinated or to remain untreated as vaccine controls. Selections were made by one of the authors (WEP) using a table of random permutations. Half of the platoons in each series were vaccinated. Thus, each treated platoon has a preselected control platoon within the same series. On the second day after arrival at MCRD, all volunteers in the platoons selected for vaccination received 0.5 ml of meningococcal vaccine[9] (6) (50 μg group C polysaccharide) in the right deltoid area using a jet hypo spray gun (Scientific Equipment Manufacturing Corp., New York, N. Y.). Only two men failed to volunteer. Pairs of vaccinated and control platoons were randomly selected (as described above) for nasopharyngeal cultural surveys. Three pairs of platoons were selected per week for nasopharyngeal culturing from the first two weeks of input and two pairs from the following four weeks of input. The men in each platoon selected had a total of five cultures approximately two weeks apart. Scheduling difficulties resulted in slightly irregular periods as shown in table 1. Nasopharyngeal cultures were taken from all men in the platoons selected for the cultural survey immediately before receiving sulfisoxazole on the

[9] Group C polysaccharide vaccine, lot No. C-7, furnished by Walter Reed Army Institute of Research, produced under contract by E. R. Squibb and Sons, Inc.

morning of the second day after arrival at MCRD. The second culture was taken between 14 and 21 days later. The three subsequent cultures were taken 9, 33 and 41 days, respectively, after the second culture. Each week initial blood specimens were collected from all men in one pair of platoons when initially cultured. Additional blood specimens were collected from the same men when the second and last cultures were taken. Continuous monitoring of outpatient visits and hospital admissions of all men in the study was performed to detect any adverse reactions to the vaccine or any evidence of meningococcal disease.

Nasopharyngeal cultures were taken and meningococci isolated and identified as previously described (7) except that sulfadiazine sensitivity was determined by inoculating Mueller-Hinton plates containing 1 mg per cent of sulfadiazine. Meningococci growing on this media were considered to be resistant to sulfadiazine. The slide agglutination test was performed using locally prepared group-specific rabbit antiserum. Meningococcal grouping antisera were absorbed with a strain of meningococci (RAS-10) which shares antigens of several serogroups, as previously described (8). The reliability of serologic identification was thereby improved. The hemagglutinating (HA) antibody tests were performed by the methods of Edwards and Driscoll (9) and the complement-fixation (CF) test by the methods of Edwards and Devine (10).

TABLE 1

Scheme of events and times

Events	Range of days Post vaccination	Median day Post vaccination
Culture-1, 1st serum vaccination	0	0
Culture-2, 2nd serum	14–21	17.5
Culture-3	23–30	26.5
Culture-4	47–54	50.5
Culture-5, 3rd serum	55–62	58.5

RESULTS

The group C meningococcal polysaccharide vaccine was administered to 3,018 Marine recruits. The effect on the carrier rates of the various serogroups in vaccinated and control men at the times of cultures during the study is shown in

TABLE 2

Distribution of per cent of Marine recruits positive for various meningococcal serogroups and sulfadiazine sensitivities at various sampling periods

Culture No.	Treatment	No. of men cultured	Per cent positive											
			C		RAS-10*		Boshard		B		Other†		Total	
			Sens.‡	Res.‡	Sens.	Res.	Sens.	Res.	Sens.	Res.	Sens.	Res.	Sens.	Res.
1	Vaccine	1056	1.6	1.8	10.4	0.4	4.0	0.6	4.6	0.6	2.8	0	23.4	3.3
	Control	1058	0.9	1.4	9.8	0.9	3.3	0.8	4.2	0.3	2.6	0	20.8	3.4
2	Vaccine	934	1.5	3.5	3.7	2.7	1.3	1.3	1.2	0.4	0.7	0.2	8.5	8.1
	Control	946	0.8	5.3	3.6	2.0	2.2	1.4	1.3	0.2	0.6	0.3	8.6	9.2
3	Vaccine	876	1.1	4.9	4.8	5.3	1.8	1.7	1.7	0.3	1.3	0	10.8	12.1
	Control	903	0.8	9.9	5.0	3.2	2.2	2.0	1.7	0.4	1.1	0.2	10.7	15.7
4	Vaccine	813	2.1	7.7	5.4	10.3	4.6	2.2	1.7	0.5	1.1	0.5	14.9	21.3
	Control	841	1.4	20.8	3.6	9.3	3.4	3.9	1.8	1.5	1.8	0.5	12.0	36.0
5	Vaccine	791	1.0	8.0	3.3	13.0	6.2	2.7	1.0	0.4	3.2	0.6	14.7	24.7
	Control	822	1.2	21.4	3.2	13.4	3.2	4.3	2.2	0.9	2.4	0.5	12.2	40.4

* Reacts to 2 or more sera.

† 29E, Z, non-typable.

‡ Sens. = sulfadiazine-sensitive; Res. = sulfadiazine-resistant.

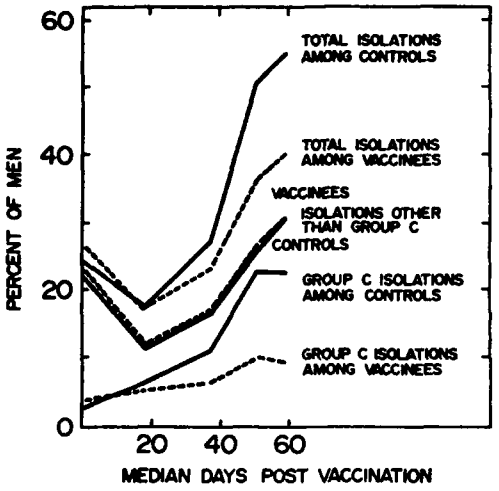


FIGURE 1. Per cent of vaccinated and control men carrying different meningococcal serogroups at median times following vaccination.

table 2. Initially, the distribution of meningococcal carrier rates in the serogroups and their sulfadiazine sensitivities were not significantly different between men in the vaccinated and control platoons. The majority of the meningococcal strains isolated on the first culture from all of the men were sulfadiazine sensitive. The effect of sulfisoxazole prophylaxis is apparent from these data. There was a marked reduction in carrier rates of sulfadiazine-sensitive organisms at the time of the second culture. Group C meningococci were initially the most prevalent sulfadiazine-resistant serogroup, and as would be expected, remained the most prevalent organism throughout the study.

The cultural data are summarized in figure 1 and show the effect of vaccination with group C polysaccharide on the meningococcal carrier rates. There was a reduction in the meningococcal carrier rate after the second culture in the vaccinated men when compared to the controls. The vaccine reduced the rate of acquisition of group C meningococci and had no effect on the acquisition rate of other serogroups. The difference in per cent of men carrying group C in the vaccinated and control platoons at the time of the first two cultures was not statistically significant. A comparison of the isolations, using the analysis of variance, showed that significantly more group C strains were isolated from the control men at the time of the third, fourth and fifth cultures than from the vaccinated men ($p = <0.05$).

The data in table 3 show the number of men in vaccinated platoons and their controls acquiring group C meningococci after the second culture. Those included in this table had five cultures taken. Comparison can be made between pairs of vaccinated and control platoons entering training in the same series. In 13 of 14 pairs of platoons, fewer vaccinated men acquired group C meningococci after the second culture than did their controls.

Sera from 20 individuals in each of six vaccinated and six control platoons were selected for a serologic survey. A series of three sera was drawn from these men at the time of the first, second and fifth cultures (table 1). Group C specific HA and genus specific CF tests were used to de-

TABLE 3

Numbers and per cents of men acquiring group C meningococci after second culture in paired vaccinated and control platoons

No. of men	Group C isolates		No. of men	Group C isolates	
	No.	(%)		No.	(%)
44	6	(13.6)	61	35	(57.4)
60	2	(3.3)	51	26	(51.0)
47	6	(12.8)	59	20	(33.9)
51	11	(21.6)	57	18	(31.6)
59	3	(5.1)	56	14	(25.0)
37	2	(5.4)	33	12	(36.4)
49	0	(0.0)	55	11	(20.0)
45	6	(13.3)	60	11	(18.3)
58	1	(1.7)	66	11	(16.7)
52	4	(7.7)	56	9	(16.1)
61	6	(9.8)	54	8	(14.8)
57	3	(5.3)	51	6	(11.8)
54	0	(0.0)	46	1	(2.2)
58	8	(13.8)	59	1	(1.7)
732	58	(7.9)	764	183	(24.0)

TABLE 4

Numbers of vaccinated or control men not carrying group C meningococci at the onset of the study who subsequently developed a fourfold or greater serologic rise at either the time of the second or third serum sample

Serologic test	Treatment	No. of men	2nd serum sample* No. (%)	3rd serum sample† No. (%)
Hemagglutination (Group C)	Vaccine	116	113 (97.4)	0 (0.0)
	Control	119	3 (2.5)	28 (23.6)
Complement fixation	Vaccine	116	0 (0.0)	6 (5.2)
	Control	119	0 (0.0)	26 (21.8)

* 14–21 days post vaccination.
† 55–62 days post vaccination.

termine fourfold or greater antibody rises. The results summarized in table 4 include only data obtained from sera of individuals who were noncarriers at the beginning of the study. Fourfold or greater HA antibody titer rises were found in 97.4 per cent of the sera of vaccinated men at the time of the second serum sample in contrast to 2.5 per cent of the sera taken from the nonvaccinated controls. The prevaccination HA antibody titers of the three vaccinated men who failed to develop a significant rise were <1:2, 1:8 and 1:256. Two of the three control men who had developed significant HA antibody titer rises to group C between the first and second sera, had become carriers of group C by the time of the second serum sample. Significant rises in HA antibody titer to group C occurred in 23.6 per cent of 119 control subjects between the second and third serum samples. This is consistent with the time and magnitude of acquisition of group C among controls as shown in figure 1. Although 97.4 per cent of the vaccinated and 2.5 per cent of the control men developed a significant rise in HA antibody titer to group C in the second serum sample, none of these men developed a significant rise in CF titer. Subsequently, in the third serum sample 21.8 per cent of the control men and 5.2 per cent of the vaccinated men developed significant CF antibody titer rises.

Table 5 summarizes the cultural and serologic results in vaccinated and control subjects during the study. Twenty-six of 34 control men who became carriers of group C developed a fourfold HA antibody titer rise to group C. Five of 31 control men who developed a fourfold HA antibody titer rise did not become carriers of group C at any time. Thus, eight carriers of group C failed to develop a significant HA antibody titer rise to group C. Only four vaccinated men who had a group C HA response to the vaccine subsequently acquired group C. None of the vaccinated men developed an additional significant antibody rise to group C at the time of the third serum sample. In those men who developed fourfold HA antibody rises following vaccination, the geometric mean of the reciprocals of their titers was increased from 2.1 to 82.7. These titers ranged from 1:16 to 1:2040.

One vaccinee had a gradual onset of polyarthritis and fever which became incapacitating with bilateral effusion of knees by the third day after vaccination. Because of a holiday weekend, he did not receive any other immunization or sulfisoxazole. He was hospitalized for a period

TABLE 5

Relationship of 4-fold or greater serologic rise and acquisition of group C meningococcus in vaccinated and control men

	No. of men	
Acquisition	Vaccinated	Control
Group C	4	34
CF* and HA† response	1	18
HA only	3	8
CF only	0	1
No seroresponse	0	7
No acquisition		
Group C	112	85
CF and HA response	5	5
HA only	104	0
CF only	0	2
No seroresponse	3	78

* Complement fixation.
† Hemagglutination.

TABLE 6

The results of nasopharyngeal meningococcal cultures taken from three men who subsequently developed group C clinical meningitis

Subjects	Days prior to onset	Result	Days prior to onset	Result	Days prior to onset	Result
RP	33	Negative	12	Negative	4	Group C
JS			21	Negative	2	Group C
LM			23	Negative	4	Negative

of 15 days with complete resolution of all signs and symptoms without specific therapy. Meningococci were not isolated from the nasopharynx on the third or 21st day post vaccination. Serum collected on the third day after vaccination had neither HA nor CF meningococcal antibody titers, but the group C meningococcal HA antibody rose to 1:32 by the 21st day after vaccination. Antistreptolysin O titers obtained on the third, sixth, 21st and 73rd days post vaccination were 96, 128, 384 and 256 Todd units, respectively. However, it was not considered that pathogenesis of the fever and arthritis were definitely established in this case. No other local or systemic reactions were noted among any other vaccinees.

There were three cases of meningococcal meningitis among the men in the control platoons in this study population. Each was of group C etiology. All of the cases fortuitously occurred in platoons preselected for the cultural survey. Table 6 shows the nasopharyngeal cultural results of the patients at various times prior to onset of clinical disease.

DISCUSSION

A group C meningococcal polysaccharide vaccine administered to Marine recruits was effective in reducing nasopharyngeal acquisition of group C meningococci. The vaccine elicited a good HA antibody response to group C in 97 per cent of the vaccinated men but failed to stimulate the production of CF antibody. Three cases of clinical meningococcal disease occurred among the more than 3,000 controls and no cases developed among a similar number of vaccinees. The vaccine was well tolerated with the exception of one person who developed an atypical illness of uncertain etiology.

Nasopharyngeal cultures were taken from the three men in the control group who subsequently developed clinical meningococcal disease. Two of these men became carriers two or more days before onset of symptoms. The third was not a carrier four days prior to illness. The significance of protecting certain individuals from acquiring meningococci is suggested by these data.

The sulfisoxazole prophylaxis program temporarily effected a significant reduction in the meningococcal carrier rate during the first two weeks of training. However, by the time of the third culture, sulfadiazine-resistant group C meningococcal strains became the most prevalent group and continued to be so among control men throughout the study.

An apparent effect of vaccination with group C polysaccharide was the inhibition of the acquisition of group C meningococci. This vaccine was obviously group-specific as evidenced by the nearly identical acquisition of meningococci of all other serogroups among vaccinated and control subjects. Gotschlich et al. (6) suggested that the reduction in acquisition of group C by vaccination may be offset by an increase in the prevalence of meningococci of other serogroups. This was not observed in this study, although only half of the incoming recruits were vaccinated for a period of only six weeks while other serogroups were prevalent.

There were marked variations between platoons in the number of group C acquisitions in this study. However, in 13 of 14 pairs observed, the men in the vaccinated platoons had fewer acquisitions of group C. The overall reduction in the acquisition

of group C by culture in the men in the vaccinated platoons was 67 per cent, which offsets the platoon variations.

Significant HA meningococcal antibody rises to group C occurred in all but three of 116 vaccinated men within two to three weeks after vaccination but none of these 116 men developed CF antibody titer rises during this time. There were no significant CF antibody rises in the final serum samples of any men in either group in the absence of the carrier state. Twenty-six of 119 control men and only six of 116 vaccinated men developed significant rises in CF antibody titers following the subsequent acquisition of one of the serogroups of meningococci. The number of CF responses following acquisition of other serogroups of meningococci was the same in vaccinated and control men. The difference noted in total CF response between vaccinated and control subjects is due to the difference in the acquisition rates of group C in the two populations. These data suggest that the CF test may be a useful tool for estimating the efficacy of this meningococcal vaccine in reducing total meningococcal acquisitions or infections. The relative reduction of CF response associated with vaccine in this study was 76 per cent and is only slightly greater than the reduction in acquisition of group C meningococci observed by culture.

The vaccine appears to be potentially useful in the control of group C meningococcal disease. The prophylactic effect of this vaccine, however, cannot be compared to the effect of sulfonamide prophylaxis. Sulfonamides eliminate the carrier state, whereas, the vaccine prevents acquisition of meningococci. Furthermore, the effect of vaccination is delayed until antibodies develop. Therefore, when epidemic disease occurs in a recruit camp early in training, the effect of vaccination on the epidemic may be limited and delayed.

There are several other important factors to consider before accepting this vaccine in routine control of disease. Consideration must be given to the fact that this vaccine is clearly group-specific. Cultural surveillance will determine the ecological consequences of group-specific vaccination. Continued use of this vaccine in a unique environment such as a military recruit camp could well give meningococci of other serologic groups a selective advantage in spreading. The use of a polyvalent vaccine would overcome this potential drawback if it should be observed.

Historically in military populations, meningococcal disease has been primarily a recruit disease. This is partially explained as the result of the intermingling of large numbers of susceptible men. Recruits may become "seasoned" by developing protective antibodies during nasopharyngeal infections. These antibodies apparently give long-term protection. It would be important to know if protection of comparable degree and duration can also be achieved by vaccination.

References

1. Lepeysonnie, L. La méningite cérébro-spinale en Afrique. World Health Organisation Bulletin 28, Supplement, 1963.
2. Goldschneider, I., Gotschlich, E. C. and Artenstein, M. S. Human immunity to the meningococcus. I. The role of humoral antibodies. J. Exp. Med., 1969, *129:* 1307–1326.
3. Goldschneider, I., Gotschlich, E. C. and Artenstein, M. S. Human immunity to the meningococcus. II. Development of natural immunity. J. Exp. Med., 1969, *129:* 1327–13
4. Gotschlich, E. C., Liu, T. Y. and Artenstein, M. S. Human immunity to the meningococcus. III. Preparation and immunochemical properties of the group A, group B and group C meningococcal polysaccharides. J. Exp. Med., 1969, *129:* 1349–1365.
5. Gotschlich, E. C., Goldschneider, I. and Artenstein, M. S. Human immunity to the meningococcus. IV. Immunogenicity of group A and group C meningococcal polysaccharides in human volunteers. J. Exp. Med., 1969, *129:* 1367–1384.
6. Gotschlich, E. C., Goldschneider, I. and Ar-

tenstein, M. S. Human immunity of the meningococcus. V. The effect of immunisation with meningococcal group C polysaccharides on the carrier state. J. Exp. Med., 1969, *129:* 1385–1395.

7. Devine, L. F., Knowles, R. C., Pierce, W. E., Peckinpaugh, R. O., Hagerman, C. R. and Lytle, R. I. Proposed model for screening antimicrobial agents for potential use in eliminating meningococci from the nasopharynx of healthy carriers. Antimicrobial Agents and Chemotherapy—1968, 1969, pp. 307–314.
8. Devine, L. F. and Hagerman, C. R. Relationship of serogroups of *Neisseria meningitidis*. I. Microagglutination, gel diffusion and slide agglutination studies of meningococcal antisera before and after absorption with RAS-10 strain of meningococci. Infect. Immun., 1970, *1:* 226–231.
9. Edwards, E. A. and Driscoll, W. S. Group-specific hemagglutination test for *Neisseria meningitidis* antibodies. Proc. Soc. Exp. Biol. Med., 1967, *126:* 876–879.
10. Edwards, E. A. and Devine, L. F. A genus-specific complement fixation antigen from *Neisseria meningitidis*. Proc. Soc. Exp. Biol. Med., 1968, *128:* 1168–1173.